II. REMARKS

A. Status of the Claims

Claims 24, 26-40, 42, 44, 45, and 61-62 are pending in the application. Claims 41 and 43 have been withdrawn from consideration, as they are drawn to non-elected species. Claims 63-68 have been added. No new matter is added by the new claims, and support for the new claims can be found in the specification and claims as originally filed. Therefore, claims 24, 26-45, and 61-68 are pending. Reentry of claims 41 and 43 in view of the allowability of claim 24 is requested below.

B. The Written Description Rejection is Overcome

The Action rejects claims 24, 26-40, 42, 44, 45, and 61 under 35 U.S.C. § 112, first paragraph for lack of written description. With regard to the amendment of claim 24 in the previous Response, the Action contends that the to the extent the deletion of the phrase "wherein the arrangement is adapted to visualize movements of molecules . . . using a single dye tracing (SDT) method" increases the scope of the claims, the increased breadth represents new matter. Applicant respectfully traverses this rejection.

The Office appears to be operating under the assumption that the phrase "wherein the arrangement is adapted to visualize movements of molecules . . . using a single dye tracing (SDT) method" was included in the claims as originally filed. This assumption is incorrect, as the phrase in question was added to claims in the Amendment and Response to Office Action Dated February 23, 2005 (which Applicant mailed on June 23, 2005). Applicant notes that the Office did not find the claims to lack adequate written description prior to the addition of the phrase in question. The deletion of the phrase in question does not increase the breadth of the

claims beyond that which the Office has already found to be adequately supported by the specification.

To the extent the Office nevertheless requires that Applicant disclose where in the specification support for the amendment can be found, Applicant respectfully directs the Office's attention to the fact that original claim 1 (upon which present claim 24 is based) does not contain the phrase in question. This is strong evidence that the breadth of the present claims does not represent new matter. *See* MPEP § 2163[II][A] (explaining that "rejection of an original claim for lack of written description should be rare"). This is because "[t]here is a strong presumption that an adequate written description of the claimed invention is present when the application is filed." MPEP § 2163[I][A]. To overcome this strong presumption, the "PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims." *In re Wertheim*, 541 F.2d 257, 263 (CCPA 1976). The Office has not met this burden, as it has not come forward with **any** evidence to support an assertion that persons skilled in the art would not recognize in the specification and original claims a description of the invention defined by the present claims.

As the foregoing illustrates, all of the claims have written support adequate to satisfy 35 U.S.C. § 112, first paragraph, and this rejection should therefore be withdrawn.

C. The Indefiniteness Rejections are Overcome

The Action rejects claims 24, 26-40, 42, 44-45, and 61-62 under 35 U.S.C. § 112, second paragraph, as being indefinite and/or unclear. The Action maintains that "the term 'large-area' [in claim 24] is a relative term, which renders the claim indefinite and/or unclear." The Action, p. 3. The Action also rejects claim 62 on the grounds that the phrase "wherein the arrangement is adapted to visualize movements of molecules . . . by using the single dye tracing (SDT)

method" is vague and indefinite. The Action, p. 3. Applicant respectfully traverses these rejections.

1. The term "large-area fluorescent excitation" is not indefinite.

In its previous Responses, Applicant presented sufficient evidence, including two declarations from a person of ordinary skill in the art, to establish that the term "large-area fluorescent excitation" is well-understood by persons of ordinary skill in the art to be synonymous with the term "wide-field illumination," a method in which "a large area of between 100 μm^2 (the size of a single biological cell) to 10,000 μm^2 is evenly and simultaneously illuminated while its image is recorded." Declaration of Dr. Max Sonnleitner Under 37 CFR 1.132 (Appendix A to June 23, 2005 Amendment and Response).

The Office contends that Applicant's evidence is insufficient, in part, because none of the three references cited in the Supplemental Sonnleitner Declaration specifically uses the term "large-area fluorescent excitation," and thus those references "could not possibly be used to prove its meaning." The Action, p. 7. Applicant respectfully notes that the ultimate question in this rejection is whether, in the art of fluorescence microscopy, "large-area" is a relative term when it is used to modify "fluorescent excitation." The references cited by Dr. Sonnleitner are instructive on this question, as they all involve use of the phrase "large-area" in the context of fluorescent excitation.

As explained in Applicant's previous Responses and in the Sonnleitner declarations submitted by Applicant, to those of skill in the art of fluorescence microscopy, the term "large-area" is **not** a relative term when it is used to modify "fluorescent excitation." Rather, the term "large-area" is used to distinguish the light source used in non-confocal microscopy (*i.e.*, wide-field microscopy) from the light source used in confocal microscopy (in which illumination is performed pixel-wise, i.e., on a spot, rather than over a "large area" or "wide-field").

While they do not use the exact term "large-area fluorescent excitation," the references cited by Dr. Sonnleitner are instructive on the definiteness question. They establish that those of skill in the art of fluorescence microscopy frequently use the terms "large area" and "wide-field" not in a relative sense but rather to describe the illumination or fluorescent excitation of samples in a non-confocal manner.

To cast doubt upon the objective truth of the Sonnleitner declarations, the Office cites to a reference by Li, *et al.* The Office contends that Li supports the proposition "that a person of skill in the art would understand that 'large areas' can be excited using confocal imaging." The Action, p. 7. Applicant respectfully notes that the Office's characterization of the teachings of Li is incorrect. As Li establishes, in wide-field microscopy (*i.e.*, large-area fluorescent excitation), "the entire field of view is uniformly illuminated and observed." Li, p. 2. Conversely, in confocal microscopy, "both the illumination and the detection are confined to a diffraction-limited spot." *Id.* Thus, as Li establishes, in confocal imaging only a "spot" (as opposed to a "large area" or a "wide-field") is illuminated at a given point in time.

To support its characterization of Li, the Office cites a passage from Li that the technique disclosed therein "is capable of confocal imaging of large area specimen in a single scan . . . ." A person of ordinary skill in the art would not understand from this disclosure that "large areas" can be excited (*i.e.*, illuminated) using confocal imaging. By definition, in confocal imaging, illumination is performed pixel-wise, *i.e.*, on a spot, rather than over a "large area" or "wide-field."

The fact that the technique of Li is capable of **imaging** a "large area in a single scan" does not mean that **illumination** in Li's technique is not confined to a diffraction-limited spot. If that were true, the technique of Li would not be referred to therein as a "confocal" imaging

technique. In describing its confocal system, Li confirms that its technique involves the illumination of a spot rather than a large area: "The raster scan of the **focused laser spot** across the specimen is realized by scanning in the X (lateral direction) and stage scanning in the Y (longitudinal) direction of the specimen . . . ." Li, p. 5.

2. *The phrase "wherein the arrangement is adapted to visualize movements of molecules . . . by using the single dye tracing (SDT) method" is not indefinite.*

In its previous Responses, Applicant established that the term "wherein the arrangement is adapted to visualize movements of molecules . . . by using the single dye tracing (SDT) method" would be well-understood by persons of ordinary skill in the art. The Office has failed to establish otherwise.

While the Office attempts to distinguish this case from *Ex Parte Porter* on the grounds that *Porter* "addressed the term 'utilizing' not the currently claimed 'use' language," the Office has not provided any substantive rationale as to why the principles of *Porter* do not apply to this case. The terms "utilize" and "use" are synonyms. *See Roget's New Millennium Thesaurus*, First Edition. Thus, as established by *Porter*, the Office cannot hold claim 62 indefinite solely on the basis that it recites "using" language.

The term "by using the single dye tracing (SDT) method" modifies the structural limitation "adapted to visualize movements of molecules." As the SDT technique is discussed in great detail in the specification, a person of skill in the art would understand the claim when it is read in light of the specification. *See In re Moore*, 439 F.2d 1232, 1235 (CCPA 1971) ("The definiteness of the language employed must be analyzed--not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art.").

The Office once again mischaracterizes Applicant's previous statements regarding Schmidt. What Applicant actually stated in the June 23, 2005 Response was that Schmidt "does not teach the visualization of movements of molecules, interactions between molecules, and molecular processes **within a three-dimensional biological cell or cells**; it only discloses artificial flat-surface lipids." Response dated 6/23/05, p. 17 (emphasis added). Thus, Applicant never "admitted" that SDT methods could not be used to visualize movements of molecules, interactions between molecules, and molecular processes in a sample. To the contrary, Applicant has consistently maintained that SDT methods can be used to visualize movements of molecules, interactions between molecules, and molecular processes in a sample, a fact which is easily understood by a person of ordinary skill in the art.

As set forth above and in Applicant's previous Responses, the rejections of claims 24, 26-40, 42, 44-45, and 61-62, as being indefinite and/or unclear are overcome and should be withdrawn.

D. The Anticipation Rejections are Overcome

The Action rejects claims 24, 26-28, 30-34, and 61-62 under 35 U.S.C. § 102(b) as being anticipated by Sharonov. The Action rejects claims 24, 26, 27, 30, 32, 34, 35, 37, and 61 as being anticipated by Sanchez. Applicant respectfully traverses both of these rejections. For the reasons set forth below and in Applicant's previous Responses, neither Sharonov nor Sanchez teaches any of the following three elements of the claims: (1) a light source configured for use in large-area fluorescent excitation, (2) a control unit adapted to coordinate and synchronize illumination times and lateral movement, and (3) an arrangement adapted to visualize movements . . . by using a single dye tracing (SDT) method.

1. Sharonov and Sanchez do not teach "a light source configured for use in large-area fluorescent excitation."

As explained in the previous Responses, because Sharonov and Sanchez are directed solely to **confocal** microscopy, they no do not anticipate the present claims. This is because confocal microscopy is completely different from the large-area fluorescent excitation technique recited by the present claims.

The Office contends that "[s]ince 'large area' fluorescent excitation does not require the use of 'simultaneous' excitation, both the 'single scan' and the 'tiling process' [described in the Li reference] would read on Applicant's claims." To the extent the Office is asserting that **any** teaching in Li anticipates Applicant's claims, Applicant notes that Li was published over four years after Applicant's priority date and is therefore not prior art to the present application. Furthermore, as established by the declaratory evidence previously submitted by Applicant, persons of ordinary skill in the art understand that large-area fluorescent excitation **does** require the use of simultaneous excitation, and thus the Office's arguments to the contrary are incorrect.

Because Sharonov and Sanchez do not teach a light source configured for use in large-area fluorescent excitation, they do not teach or suggest each and every element of the present claims. Thus, the anticipation rejections cannot be maintained and should be withdrawn.

2. Sharonov and Sanchez do not teach "a control unit adapted to coordinate and synchronize illumination times and lateral movement."

As explained in the previous Responses, neither Sharonov nor Sanchez teaches a control unit adapted to coordinate and synchronize illumination times and lateral movement. The Office's assertion that this limitation does not constitute a limitation in any patentable sense is contrary to established law. The Federal Circuit has afforded patentable weight to elements "adapted to" perform a function. *See, e.g., Pac-Tec, Inc. v. Amerace Corp.*, 903 F.2d 796, 801 (Fed. Cir. 1990). Applicant's further disagree with the Office's contention that this limitation

constitutes an intended use and therefore does not warrant patentable weight. Stating that a structure is "adapted to" perform a specific function is an acceptable means of defining a structure. *See id.*

The control unit of the present claims is described in the articles "Ultra-sensitive DNA Detection on Microarrays" by Jacak, *et al.*, Proc.Spie 5699 (2005) 442-449 ("Jacak") (attached hereto as Appendix A) and "A fast Scanner for Fluorescence Microscopy Using a 2-D CCD and Time Delayed Integration" by Netten, *et al.*, Bioimaging 2 (1994) 184-192 ("Netten") (attached hereto as Appendix B), which describe the control unit of the present claims as operating in time delayed integration (TDI) mode. That the control unit of the present claims is adapted for operating in TDI mode is also disclosed in the present specification at pp. 8-9 ("the control unit can also coordinate and synchronize the positioning and the shifting of the images to each sample position on the pixel array of the CCD camera and control and coordinate the readout and the evaluation of the pixel array images").

Neither Sharonov nor Sanchez discloses a control unit adapted to operate a CCD camera in TDI mode (*i.e.*, adapted to coordinate and synchronize illumination times and lateral movement between said sample holder and said detection and analysis system during use), nor do they disclose that the TDI mode is used for controlling a sample holder. As acknowledged by the Action, Sharonov merely states, "The scanning of the sample stage and mirrors of the optical scanner and all operations connected with recording of spectra are computer-controlled . . . ." The Action, p. 23. A disclosure that scanning operations are "computer-controlled" does not amount to the teaching of a controller adapted to **coordinate** and **synchronize** illumination times and lateral movement. The Action asserts that Sanchez's disclosure that "a modified Nanoscope IIIA controller was used for controlling the scan bed and image acquisition" (The Action, p. 23)

amounts to the teaching of a controller adapted to coordinate and synchronize illumination times and lateral movement. The disclosure that a "controller" was used for controlling the scan bed and image acquisition does not amount to the teaching of a controller adapted to **coordinate** and **synchronize** illumination times and lateral movement.

Because Sharonov and Sanchez do not teach a control unit adapted to coordinate and synchronize illumination times and lateral movement, they do not teach or suggest each and every element of the present claims. Thus, the anticipation rejections cannot be maintained and should be withdrawn.

3. Sharonov and Sanchez do not teach "wherein the arrangement is adapted to visualize movements of molecules . . . by using a single dye tracing (SDT) method."

As explained in the previous Responses, neither Sharonov nor Sanchez teaches an arrangement that is adapted to visualize movements of molecules by using a single dye tracing (SDT) method. The Office's assertion that this limitation does not constitute a limitation in any patentable sense lacks merit. As explained above, the Federal Circuit has afforded patentable weight to elements "adapted to" perform a function.

Because Sharonov and Sanchez do not teach an arrangement that is adapted to visualize movements of molecules by using a single dye tracing (SDT) method, they do not teach or suggest each and every element of present claim 62, and claim 62 is thus allowable.

E. The Obviousness Rejections are Overcome

1. Claims 24, 26-27, 29-30, 32, 34-35, 37, 44, and 61-62 are not obvious over Sanchez and Lewis.

The Action rejects claims 24, 26-27, 29-30, 32, 34-35, 37, 44, and 61-62 under 35 U.S.C. § 103(a) as being obvious over Sanchez in view of Lewis. Applicant respectfully traverses.

As explained in detail above (with regard to Sanchez) and in the previous Responses (with regard to Sanchez and Lewis), the cited references do not teach all of the limitations of the rejected claims. Neither Sanchez nor Lewis teaches (1) a light source configured for use in large-area fluorescent excitation, or (2) a control unit adapted to coordinate and synchronize illumination times and lateral movement. For at least these reasons, a *prima facie* case of obviousness has not been established. *See In re Vaeck*, 947 F.2d 488, (Fed Cir. 1991). The rejection of claims 24, 26-27, 29-30, 32, 34-35, 37, 44, and 61-62 as obvious over Sanchez and Lewis should therefore be withdrawn.

2. *Claims 24, 26-40, 42, 44-45, and 61-62 are not obvious over Schmidt-1, Schmidt-2, Lewis, Al-Ghoul, and Albertine.*

The Action rejects claims 24-40, 42, 44-45, and 61-62 under 35 U.S.C. § 103(a) as being over Schmidt, *et al.* "Imaging of single molecule diffusion") ("Schmidt-1"), as evidenced by Schmidt, *et al.* "Microscopy for Recognition of Individual Molecules" ("Schmidt-2"), Lewis, Al-Ghoul, and Albertine. Applicant respectfully traverses.

As explained in the previous Response, Schmidt-1 does not teach a control unit adapted to coordinate and synchronize illumination times and lateral movement between a sample holder and a detection and analysis system during use. As in the previous Office Action, the Office once again does not even assert that Schmidt-1 teaches a control unit adapted to coordinate and synchronize illumination times **and lateral movement**, instead merely arguing that Schmidt-1 teaches "a control unit adapted to coordinate and synchronize illumination times." The Action, p. 31.

The Office's assertion that the limitation "a control unit adapted to coordinate and synchronize illumination times and lateral movement" does not constitute a limitation in any patentable sense lacks merit. As explained above, the Federal Circuit has afforded patentable

weight to elements "adapted to" perform a function. Applicant's further disagree with the Office's contention that this limitation constitutes an intended use and therefore does not warrant patentable weight. Stating that a structure is "adapted to" perform a specific function is an acceptable means of defining a structure.

An explanation of the differences in the sequential recording system of Schmidt-1 and the TDI system of the present claims is found in the article "Single-Molecule Reader for High-Throughput Bioanalysis" by Hesse, *et al.*, Anal.Chem. 76 (2004):5960-5964 ("Hesse-3") (attached hereto as Appendix C). The system of Schmidt-1 is described therein as a "conventional microscope-based system" that acquires sequential images in order to cover large areas. Hesse-3, p. 5960, col. 2. With sequential recording devices such as the one in Schmidt-1, inertia of the moving parts requires time-consuming feedback loops for precise stops, limiting the overall readout speed. *Id.* at p. 5961, col. 1. In contrast, the system of the present claims is described as "a scanning system that avoids overhead times due to both stage positioning and illumination, based on the implementation of synchronized continuous stage-shift and camera readout." *Id.* The system of the present claims achieves this effect by operating the camera in TDI mode. *Id.*

None of the cited references discloses a control unit adapted to operate a CCD camera in TDI mode and synchronize sample movement during the scanning process (*i.e.*, adapted to coordinate and synchronize illumination times, signal integration, and lateral movement between said sample holder and said detection and analysis system during use), nor do they disclose that the TDI mode is used for controlling a sample holder.

Applicant further notes that in Schmidt-1, a visualization of single molecules during movement is not possible, particularly because he sample movement in Schmidt-1 only measures on very small areas (11x11 μm^2).

For the reasons set forth above and in the previous Responses, the cited references do not teach all of the limitations of the rejected claims. Thus, a *prima facie* case of obviousness has not been established. The rejection of claims 24-40, 42, 44-45, and 61-62 as obvious over Schmidt-1 as evidenced by Schmidt-2, Lewis, Albertine, and Al-Ghoul should therefore be withdrawn.

F. The Newly Added Claims Are Allowable

Newly added claims 63-68 are allowable for over the cited art for the reasons explained above and in the previous Responses. These new claims are described in detail below.

Claim 63 is based on present claim 24, with the term "wide-field illumination" substituted for "large-area." As explained in the Sonnleitner declarations attached to Applicant's previous Responses, these terms have the same meaning to persons of ordinary skill in the art. Furthermore, as explained in the Supplemental Sonnleitner Declaration, the German word "großflächig," which was used in the original, un-translated priority document, may be translated in English as either "large-area" or "wide-field."

Claim 64 is based on present claim 24, with the specific fluorescent excitation area size of 100 to 100,000 μm^2 substituted for the term "large-area." This recitation is supported by the specification at, for example, page 7.

Claim 65 is based on present claim 24, with the phrase "and vertically" inserted after "movable laterally" and the word "vertical" inserted before "movement between said sample holder." These recitations are supported by the specification at, for example, page 7.

Claim 66 is dependent from new claim 65 and recites that lateral and vertical movement is controlled by a piezo element. This recitation finds support in the specification at, for example, page 22.

Claim 67 incorporates present claim 31 into present claim 24, and claim 68 incorporates present claim 36 into present claim 24.

G. Entry of Non-elected Species Is Requested

In view of the foregoing arguments, all the presented claims are in condition of allowance. Thus, all species contained in the dependent claims withdrawn by the examiner (claims 41 and 43) should be reentered into the case and allowed.

H. Conclusion

Applicant believes that the foregoing remarks fully respond to all outstanding matters for this application. Applicant respectfully requests that the rejections of all claims be withdrawn so they may pass to issuance.

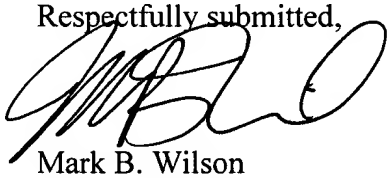
III. REQUEST FOR EXTENSION OF TIME

Pursuant to 37 C.F.R. § 1.136(a), Applicant petitions for an extension of time of three months to and including January 5, 2007, in which to respond to the Office Action dated July 5, 2005.

Pursuant to 37 C.F.R. § 1.17, a check in the amount of $510.00 is enclosed, which is the process fee for a three-month extension of time for a small entity status. If the check is inadvertently omitted, or should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, or should an overpayment be included, the Commissioner is authorized to deduct or credit the appropriate fees from or to Fulbright & Jaworski Deposit Account No. 50-1212/SONN:010US.

The Examiner is invited to contact the undersigned Attorney at (512) 536-3035 with any questions, comments, or suggestions relating to this patent application.

Respectfully submitted,



Mark B. Wilson
Reg. No. 37,259
Attorney for Applicant

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
(512) 536-3035

Date: December 20, 2006